

REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments and remarks herein, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-7 and 10-18 are pending in this application. Claim 6 has been amended to correct a typographical error. Support can be found in paragraphs 0133 and 0134 of the specification as published. Claim 18 has been rewritten in independent form according to the Examiner's suggestion. No new matter has been added.

The Examiner is thanked for vacating the restriction requirement.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. §112. It is submitted that the amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

The issues raised by the Examiner in the Office Action are addressed below in the order they appear in the prior Action.

II. CLAIM OBJECTIONS ARE OVERCOME

Claim 18 is being objected as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all the limitations of the base claim and intervening claims.

Claim 18 has been rewritten in independent form thereby obviating the objection.

Reconsideration and withdrawal of the claim objections are respectfully requested.

III. THE REJECTIONS UNDER 35 U.S.C. §112 ARE OVERCOME

Claims 1-6 and 10-17 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for certain compounds of formula (I), or composition thereof,

and a method of making and using said compounds and compositions, allegedly does not reasonably provide enablement for all other compounds encompassed by the claims. The Examiner further asserts that the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The Examiner concludes that “undue and unpredictable experimentation would be required”. Applicants traverse the rejection.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988),

Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is undue, not experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted]. *Id.* at 1404.

The Examiner is respectfully reminded that considerable experimentation is permissible if said experimentation is routine or if the specification provides reasonable guidance with respect to the direction in which experimentation should proceed.

The invention relates to 5-substituted-oxyalkylaminopyrazole derivatives of formula (I) or salts thereof, to process for their preparation, to compositions thereof, and to their use for the control of pests.

Applicants respectfully assert that when read in view of the specification, the pending claims are enabled.

The present specification describes the methods for the preparation of the compounds of general formula (I) as known, i.e., “methods heretofore used or described in the chemical literature” (paragraph 0125 of the specification as published). Furthermore, paragraphs 0127-

0144 relate to the detailed synthetic methods for the preparation of compounds of formula (I) and their intermediates. As stated in paragraph 0145, compounds of formulas (III)-(XI) “are known or may be prepared by known methods”. Therefore, provided the skill level of an ordinary skilled artisan is high and the level of predictability in the art is high, the preparation of the claimed compounds from the known intermediates does not require undue and unpredictable experimentation as it involves known and reliable synthetic procedures. Therefore, all the claimed compounds are enabled by the specification, and not just the exemplified compounds as alleged by the Examiner. “Limitations and examples in the specification do not generally limit what is covered by the claims”. MPEP 2164.08.

The Examiner further alleges that the instant claims are drawn to an exceedingly vast and diverse range of compounds and that any one compound would not be necessarily an obvious variant of another compound selected from the same possible substituents.

Paragraphs 0133-0134 of the specification as published provide sufficient guidance and direction for the preparation of compounds of formula (I) where R^1 is $C(=NZ)S(O)_r-Q$ from the compounds of formula (I) where R^1 is $CSNH_2$. The compounds where R^1 is $C(=NZ)S(O)_r-Q$ or $CSNH_2$ are obvious variants of compounds exemplified in the disclosure as they belong to the same class of 5-substituted-oxyalkylaminopyrazole derivatives of formula (I) as the compounds with R^1 being a cyano group. Compounds of formula (I) where the R^1 is $C(=NZ)S(O)_r-Q$ or $CSNH_2$ are prepared from the same intermediate of formula (II) using methods described in the specification and known in chemical literature. Compounds with various R^4 and R^5 groups are also obvious variant as they all possess the same 5-substituted-oxyalkylaminopyrazole core structure. Contrary to the Examiner’s assertion, compounds of formula (I) are all 5-oxyalkylaminopyrazole derivatives, which can be prepared from the same intermediate of formula (II) having the 5-oxyalkylamino-1-arylpyrazole core structure.

The Examiner further contends that the Applicant has failed to provide any data suggesting that any molecule other than the small disclosed subset of compounds would be an effective pesticidal compound, and therefore one of ordinary skill in the art could not reasonably determine whether the claimed compounds would be effective pesticides.

Applicants respectfully submit that the presently claimed compounds are C-5 modified derivatives of the previously presented compounds which were found to be effective as pesticides. Introduction of the novel C-5 moiety further improves the pesticidal properties of the

pesticides. Introduction of the novel C-5 moiety further improves the pesticidal properties of the previously disclosed compounds. The presently disclosed novel 5-substituted-oxyalkylamino-1-arylpyrazole pesticides may be used in oral form (paragraph 0005 of the specification as published), at a lower dose than the existing pesticides (paragraph 0006), are substantially non-emetic (paragraph 0007) and are safer to the user and the environment (paragraph 0008).

Therefore, based on the description and examples presented in the specification, one skilled in the art would be able to predict that all presently claimed 5-substituted oxyalkylamino-1-arylpyrazole derivatives would have improved pesticidal properties as they all share the same core structure and are all obvious variants of the compounds exemplified in the disclosure.

Therefore, the skilled artisan would be fully enabled to practice the said invention in view of the present description.

In view of the statements above, the breadth of the claims is not unduly broad, the amount of direction provided by the instant specification is high particularly in regard to the inclusion of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure is therefore low and, in any event, would not constitute undue experimentation.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are respectfully requested.

III. THE 35 U.S.C. §103 REJECTIONS ARE OVERCOME

Claims 10, 11, 13, and 14 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kando, *et al.* (U.S. Patent No. 6,316,477) in view of Phillips, *et al.* (European Patent No. 0 500 209, 1997), Jensen-Korte, *et al.* (U.S. Patent No. 4,971,989), Manning, *et al.* (International Application WO98/28279), Wu and Pilato (U.S. Patent No. 5,691,333), and King (Medicinal Chemistry; Principals and Practice, 1994). Applicants traverse this rejection.

The Examiner is respectfully reminded of the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). As stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the

reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

Furthermore, the Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: “[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.” *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727.

Applying the law to the instant facts, the references relied upon by the Office Action do not render Applicants' invention obvious.

The present invention discloses novel 5-substituted-oxyalkylamino-1-arylpyrazole pesticides which may be used in oral form (paragraph 0005 of the specification as published), at a lower dose than the existing pesticides (paragraph 0006), which are substantially non-emetic (paragraph 0007) and which are safer to the user and the environment (paragraph 0008).

The Office Action alleges that the cited references teach a method of treating surfaces, plants, and/or animals with 1-arylpyrazole derivatives to control pests. The Examiner asserts that the fundamental difference between the compounds described in the references and the presently claimed compounds is that the $-C(C=O)OR$ residue at the 5 position of the pyrazole ring is replaced with a $-OC(=O)OR$.

The Examiner further contends that “(o)ne of ordinary skill in the art would reasonably expect that the consequent compounds would maintain their pesticidal faculties” and it would be obvious “to use the compounds and compositions of formula (I) for the treatment of loci (i.e. plants) and animals to control pests, given the close similarity of the claimed compounds and compositions to those of the prior art, as taught by Kando, *et al.*, Phillips, *et al.*, Jansen-Korte, *et al.*, Manning, *et al.*, and Wu and Pilato.

The Examiner alleges that the references teach compounds with “a $-CN$, halogen, $-C(=NY)X$ or $-C(=S)-NR$ at 3 position of the pyrazole ring” and “various substituents at the 5 position of the pyrazole ring”. The Examiner refers to the compounds by Kando, *et al.*, where

“substituents include -NH_2 , -NHCH_3 , $\text{-NHCH}_2\text{CH}_3$, -N=CHCH_3 , -NHAc , and $\text{-N(CH}_2\text{Ph)}_2$, among others”. Applicants respectfully submit that the recited C-5 substituents of Kando, *et al.* do not relate to C-5 substituents of the claimed compounds as they lack the novel substituted oxyalkyl moiety at C-5 amino group of the pyrazole ring. Moreover, Kando, *et al.* does not relate to the compounds having the claimed R^1 substituents at C-3 position of the pyrazole ring. Therefore, Kando, *et al.* does not teach or suggest the compounds of the present invention.

Phillips, *et al.* relates to 1-pyridylpyrazole compounds wherein the Y substituent at C-5 position does not represent the presently claimed substituted oxyalkylamino moiety.

Jensen-Korte, *et al.* relates to compounds with only hydrogen or alkyl at C-3 position (corresponding to the present R^1 substituent), which are not present in the disclosed compounds and also does not relate to the presently claimed substituted oxyalkylamino moiety at C-5 position of pyrazole ring.

Wu and Pilato and Manning, *et al.* also do not relate to the presently claimed substituted oxyalkylamino moiety at C-5 position.

The replacement of -C(C=O)OR residue at C-5 position of the pyrazole ring with a -OC(=O)OR is not an obvious modification based on the teachings of the cited references as none of them suggests the desirability of such modification and does not relate to the intermediates shown in the present specification used for the preparation of the claimed compounds.

The Examiner asserts that “King teaches that -O- and $\text{-CH}_2\text{-}$ are bioisosteres, so one of ordinary skill in the art would not expect that changing a methylene to ether would affect the pesticidal ability of the resultant compound”. Contrary to the Examiner’s assertion and King’s teaching, the present modification is not an introduction of an ether, but rather chemically and biologically different -O-X-Y-R^5 moiety, where oxygen is not connected to another carbon as in ether structure but to -X- , which can be -C=O , -C=S or SO_2 , which is further connected to -Y- , which is O, NR^{11} or a covalent bond. Therefore the whole functional group has to be compared to methylene and not just one oxygen. The oxygen in the presently introduced substituted oxy group represented as -O-X-Y-R^5 is not a methylene bioisostere, and therefore the properties of the compounds having this substituent cannot be predicted based on the teachings of King.

Furthermore, none of the references relates to the activity of substituted oxyalkylamino pyrazole derivatives against fleas. None of the references, except Jansen-Korte, *et al.*, relates to

the use of the described compounds against the species disclosed in paragraph 0172 of the present specification. Moreover, none of the references relates to the use of the described compounds to provide a non-emetic pesticide (as the previously known arylpyrazoles were known to cause emesis when administered orally to the animals).

As such, one skilled in the art would not be able to predict the modified compounds of the present invention, the process for their preparation, compositions and use thereof in view of the references presented by the Examiner.

For the foregoing reasons, the cited references, either alone or in combination, do not render the pending claims *prima facie* obvious.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully requested.

REQUEST FOR INTERVIEW

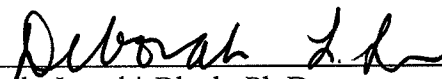
If any issue remains as an impediment to allowance, prior to issuance of any paper other than a Notice of Allowance, an interview, is respectfully requested with the Examiner, and the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the remarks and amendments herein, and prompt issuance of a Notice of Allowance is respectfully requested.

Respectfully submitted,
MERIAL LTD.
FROMMER LAWRENCE & HAUG LLP

By:



Judy Jarecki-Black, Ph.D.
Reg. No. 44,170
Tel. No. (678) 638-3805
Fax No. (678) 638-3350
Thomas J. Kowalski
Reg. No. 32,147
Deborah L. Lu, Ph.D.
Reg. No. 50,940
Tel. No. (212) 588-0800
Fax No. (212) 588-0500